

REMARKS ON HUMAN CLONING (by Maxine Singer)

COMMITTEE ON SCIENCE AND HUMAN VALUES

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apologize
for mistaken
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It is my real pleasure to be visiting with the Committee on Science and Human Values again. As some of you know, I met with the Committee for some years, as a consultant, trying to provide, when relevant, information on the progress of modern biological research. My recollections of those meetings are of rigorous, interested^{ing} and very cordial discussions. Because the Bishops' perspectives were, largely, quite different from my own, I no doubt learned more from the Committee than it learned from me.

Mike Kaback.

A great deal has been written about human cloning in the scientific and popular press and also in the various publications of your church. I don't want to spend too much time going back over the same ground again in the same context. I will spend just a few minutes being sure that we are all talking about the same thing. Then, I will try to look at the topic from the scientific point of view. I do this because I assume my job is to inform you about the way scientists look at this issue. The ideas I will present are not necessarily points of view that I myself advocate. My purpose is to provide constructive insights.

What is human cloning? The principles and the definition are essentially the same as those that Dr. Neal First has already described for other animals. Humans are one species of mammals and human biology is, in broad outline and many specifics, the same as that of any mammal. But human biology also has unique features, as does the biology of any other mammal such as mice, sheep, and cows. For example, we know that drug trials in experimental animals do not always reliably predict the effects in humans. Our cognitive and language skills are unique features of *Homo sapiens*. Similarly, ^{also} we know that the mouse and human genomes have many similarities and many differences, the significance of which should be informed by the work of the various Genome Projects. The point is, that we should expect the precise details of successful cloning of whole human organisms, should it ever be tried, to differ from those required for the cloning of other mammals. Nevertheless, given the success with cloning several mammalian species thus far, it is likely that human cloning is feasible and would work.

Before going on, it is important to provide a cautionary word about the term 'cloning'. This may seem esoteric, but as institutions and people draft policy statements, legislation or regulations, it is easy to say more than intended unless the words are rigorously used. Scientists define the word clone or cloning in a variety of ways, for example to make one or more identical organisms asexually, but fundamentally it means making identical copies of DNA. The DNA can be a single gene, a whole genome contained in single cells, or, when a whole organism is cloned, the trillions of copies of a whole genome that are present in the trillions of cells in the organism -- a mouse or a

~~Also~~ ^{Strictly speaking}
human being. ^{Scientifically} it is probably incorrect to equate somatic cell nuclear transfer with cloning an organism. To reproduce a whole organism would mean ^{on-the-spot, so to speak} constructing a whole new adult organism. What nuclear transfer techniques do is start a new developmental program leading to an organism with the same DNA as the donor. But because development is strongly influenced by environmental factors, the adults will not be identical. This may seem like splitting hairs, but, as you will see, the distinction has serious implications.

Cloning is not new. Clones of plants have probably been made from the earliest days of human history; that is what you do if you root a leaf, for example, and let it grow into a new plant. . Each of us is in a sense constructed of a population of clonal cells that arose from a single fertilized egg by ^{cell division, that is by} asexual reproduction; each cell has the same genome. Scientists have been making clones of viruses and bacterial cells ^{many} for decades. For almost as long they have been making clones of individual cells from complex organisms, including humans, in laboratory dishes. Since the mid-1970's they have been ^{First} cloning individual genes; that is what the recombinant DNA technology permitted. And, as you heard from Dr. First, for some time now, scientists have been making clones of whole experimental or agricultural animals, primarily using embryonic or fetal cells as the donors of the nucleus and its DNA. The new development is the use of adult cells to provide the donor nucleus. That is why Dolly surprised us. However, for our discussion today, I will assume that the donor of the genetic information may be a fetal cell, an embryonic cell, or an adult cell. ^{notwithstanding that it's often important} ~~It is, I think~~ important when considering the

issues associated with human cloning, to keep in mind which of these three is discussed.

Some matters of concern are unique to the use of adult donor genomes.

Issues in thinking about cloned humans. The idea of making whole human clones troubles all of us, scientists, and nonscientists alike. Scientific societies have been unanimous in calling for at least a 5 year moratorium on using SCNT for trying to make a human. Why? To get at that question I will try to distinguish between those issues which are scientifically valid and those which are not.

- One frequently voiced objection to human cloning is to the idea of producing people with the same genomes. But that happens in nature and we accept it.

Human clones are themselves ancient, probably as ancient as our species ^{and} because about ~~1~~ 0.25

percent of human ^{births} pregnancies yield identical twins, which are clones ~~(another estimate~~
~~read says one in 400 births, or 0.25 percent, in the US, Lewontin).~~

Lee Silver estimates that a million pairs of newborn identical twins are born each year, worldwide. There are also a certain number of naturally occurring identical triplets and quadruplets. We have learned some very important things from ^{observing} the study of natural human clones. We know that they are not identical people. Regardless of identical genomes, twins are

^{individuals,} independent ~~people~~. They grow into different adults depending on environmental differences, both physical and cultural, ^{differences} that start during gestation; even the environment in the uterus is different for each twin. To assume that a cloned individual would be the same person as the donor of the nucleus is incorrect. Thus, scientists find it difficult to accept statements such as Dan Callahan's "engineering someone's entire genetic makeup would compromise his or her right to a unique identity". They would also disagree with

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the assumptions made by Leon Kass, in his essay 26 years ago and summarized by George F. Will to the effect that connections with parents, siblings, and ancestors would be compromised for a clone, and that individuality, identity, and dignity cannot be severed from genetic distinctiveness and from a belief in a person's open future. We know that this is incorrect from the experience of twins. We also know that it is the parenting a child gets that establishes familial connections and that encourages individuality and dignity. We know from many many examples that parents frequently fail in these respects. There is no reason to believe that the parents of clones will do any better or worse. As a general point, if we assumed that identical genomes make two individuals identical people, we would be saying, in a sense, that humans are ~~Scientists do not subscribe to that idea~~ indistinguishable from other animals. More to my point, such an assumption is scientifically wrong because it ignores the interactions between genes and environment that are fundamental biological processes. In other words, the so-called nature-nurture debate is not an issue for science; it is settled; it is both. What is not fully known is the extent to which each of these, nature and nurture, contribute to individual traits. To summarize, it makes no sense from a scientific perspective to say, as some have, that human cloning would seriously affect the reality ~~perception~~ of what it means to be a human being. Similarly, it should not affect the perception of what it means to be human.

- Another objection to cloning is the ~~perception~~ ^{idea} that the parentage of the clone is ambiguous. Parentage would certainly be complicated, but scientifically, it's not ambiguous. The biological parents are the parents of the donor of the nucleus. The nurturing parent or parents are first the woman who gives birth to the child and then those who raise the child.

- Another objection that is not scientifically pertinent is the notion that human reproduction is God's domain, that cloning humans would be 'playing God'. Science cannot contribute to discussions of this position. Scientists are not the ones to define God's domain though some scientists are knowledgeable about theology and would have useful perspectives. The scientific perspective, however, is one that is defined by and includes only physical phenomena—things that can be observed, measured, tested, and interpreted on the basis of what we call the natural world. However, as informed citizens, scientists do, from the scientific perspective, make observations on the views of religious people and authorities. Two such observations ^{come to mind} ~~are pertinent~~.

The first is that authorities from the different religions in our plural society take quite different views of the acceptability of human cloning. The second is that since time immemorial—at least since Prometheus determined that humans should have fire, religious communities have seen new scientific concepts and capabilities as violating God's domain. In so doing they have met the resistance of the societies they serve because those societies have generally been pragmatic in confronting their own self-interests.
- Still another scientifically important point is alluded to by Dave Byers ^{his} ~~in the~~ very interesting paper included with the materials for this meeting. He says that clones would not “share fully in the mystery of human variability”. For a scientist, human variability is not a mystery. It is a consequence of the genetic mechanisms associated with sexual reproduction. From the scientific perspective, the chance mixing of genes by sexual reproduction is one of the great inventions of evolution. ~~And the~~

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scientific view agrees with that expressed by Byers in concluding that we should not

lightly tamper with these mechanisms. Byers position is consistent with my

understanding of the long-standing acceptance of biological evolution by your

church. The scientific import of the argument, however, must hinge on the

anticipated magnitude of the problem. I believe it would not be large. For many

reasons, the overwhelming majority of children born on the planet will ^{always} be the result

of natural conjugation.

- Another objection has to do with the safety and reliability of nuclear transfer as a way to produce new humans. On this issue scientists, public commentators, and the National Bioethics Advisory Committee all agree. Even if we were convinced that cloning humans by nuclear transfer would work, it would be wrong to attempt it if we weren't certain that it would be safe; safe for the mother and the new child. This means that the new human being should not suffer any disease or disability as a consequence of the procedure; ~~that~~ ^{sh} it would be a normal individual in all ways. We are not now able to assure such safety. That is why virtually all scientists—excepting such clearly irresponsible and incredible people like the physicist Richard Seed---agree that for now, no one should be allowed to attempt to produce a new human being by SCNT or indeed any similar procedure using fetal or embryonic nuclear donors.

How will we ever know whether the procedure is acceptably safe without trying it? Lee Silver in his book *Remaking Eden* says that “If cloning is found to have no effect on the health or life span of experimental animals, it would be

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failures
at all stages.

reasonable to conclude that the same would hold true for human beings.” There is likely to be substantial debate over that view.

Yet another issue that troubles many people concerns the intentions of those who would undertake human cloning. A totalitarian dictator who undertook development of a cloned population is one fantasy. A vain adult who is interested in extending his or her own existence is not so fantastic. Some object to the profit motive of those who would carry out the procedure. ~~Such~~^{MS} socially unacceptable situations will need serious attention if and when human cloning proves possible. But many people will have intentions and motivations that are widely seen as good. Motives and intentions are not matters for scientific decisions. But physician scientists will need to ~~confront~~^{assist} those individuals or couples who have no other way to produce their own children. Adoption is always an option. But we know that many people have an overwhelming desire to have their own children to love and nurture. ~~and perpetuate~~^λ. Will our society decide that ~~the~~^{for individuals} disadvantages it sees outweigh this profound benefit^λ? How will the manifold differing views of society and the personal motivations of infertile people be resolved? ~~There is some question about whether a ban on safe human cloning would be constitutional.~~

So far I have been addressing the question of human cloning defined as the production of a whole new human organism. Now I will turn to the question of the research that somatic, embryonic, and fetal cell nuclear transfer could permit. This shifts the focus from individual prospective parents and children to society as a whole because the research can have important significance for health problems.

One set of such problems has to do with infertility and spontaneous abortions, what we call miscarriage. Our present knowledge about the very early development of human embryos is scanty. Anatomical knowledge has been obtained by observation of spontaneously aborted human embryos. Additional information has been gleaned from studies on pregnant women and other mammals. Yet, understanding the early events in human development is essential if we are to understand what goes wrong in the perplexing instances of infertility or the large number of spontaneous abortions of very early embryos. We don't have very good data on the frequency of such abortions. If they happen in the first 14 days after fertilization, prior to implantation, the mother is unlikely even to suspect that she is pregnant. We do know that ^{about} ~~somewhere between a~~ ~~quarter and~~ a third of all known pregnancies do not result in a full term offspring (some estimate that it is as high as 50 percent). Sometimes it is the mother's physiology that cannot support implantation. Often it is likely to be problems with the embryo and these would almost always have a genetic explanation. Overall, some estimate the total number of spontaneous abortions starting immediately after fertilization ^{at} ~~is~~ 75 percent (Silver). What genes are important in the very early embryo? If we knew, we might be in a position to design therapies. This would require research on early embryos. In the past, such research was not technically feasible. Today it is because 1) embryos can be initiated by *in vitro* fertilization and 2) there is sufficient knowledge about the genes important in the early embryos of other mammals, particularly mice, that carefully designed experiments can be planned. Initiating early development by nuclear transfer would provide additional opportunities with some unique features.

Another possible advantage for the general society is new therapies. This is highly speculative at this time because very little relevant research has been done. But it is certainly conceivable that egg cells containing a transferred nucleus could be programmed by genetic manipulation to produce whole tissues like skin, or livers, for replacement of diseased organs. These possibilities would be foregone if all such work were forbidden. Note that in this type of research there would be no intention of implanting the cells and growing a whole organism. *****

Your church and some other organized religions and individuals object to research with human embryos whether they are formed by *in vitro* fertilization or nuclear transfer. The point of view is sufficiently widely held that federally funded research with human embryos has been prohibited, by both presidential executive order and the Congress in spite of a recommendation to the contrary by a broad-based advisory panel to the NIH in 1994. Such research is, of course, essential to the development of safe and effective procedures for cloning a human or for research on infertility and spontaneous abortion or that could lead to therapies based on cloned tissues.

If the past is any predictor of the future, there will be people with justifiable and substantial reasons who will want to use this technology. We should recall that organ transplants were considered alarming at the start but now we accept them (Steve Jones), for personal reasons and societal reasons. We will all be faced with evaluating our positions and the consequences of permitting the technology to move forward or

prohibiting it. Some of these consequences are scientific. Others are the loss of personal or societal advantages such as I have mentioned. Some of the consequences will be measured in terms of particular religious or philosophical beliefs regarding the morality and the ethics of the technology. Even these, however, can have two sides as is best illustrated by the current situation with respect to experimentation on human embryos made by fertilization *in vitro*.

As I have said, it is illegal, by presidential executive order and by legislation, to use federal funds for such research. These restrictions reflect the sense of politicians that many in the country object to such experiments as well as the views of politicians themselves. Research done with private funds is not prohibited under these regulations. No law has been passed that would cover private work. There seems to be a sense that substantial political objections would arise from diverse directions if such a law were to be proposed, including the question of constitutionality. Whatever the reason, this situation has had consequences that are troubling both to those who would like to see the research go forward and those who favor the prohibition. Private research, as well as the therapeutic application of *in vitro* fertilization in private clinics is completely unregulated. We have all sorts of laws and the FDA for regulating availability and quality of therapeutic drugs, devices, and procedures. Nothing now protects people who are interested in assisted reproductive therapies from charlatans, from shoddy practices, from unsubstantiated promises. We have no mechanism for stopping or regulating or even reviewing research on human embryos in most states, so long as it is not done with federal funds. The polarization of our society over the questions of abortion and

reproductive rights is largely responsible for our inability to have reasonable and constructive action on these issues.

Charting public policy in a country that respects the religions and cultures of diverse groups and is, at the same time, enthusiastic in accepting the technological advances brought by science is an unpredictable and sloppy venture. The clean logical lines of neither the science nor the tenets of your church are likely to be very visible in the outcome of our national debate on various aspects of human cloning. We all need to be wary, as policy is set, of unexpected and undesirable consequences. We need to look, with understanding and good will, for sensible, workable compromises.

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